REMARKS

Claims 6 to 12 and 14 to 20 are in the application. Claim 13 has been cancelled.

Rejection under 35 USC § 112

Claims 6 to 13 remain rejected under 35 USC § 112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

Claims 7 to 14 are rejected under 35 USC § 112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully traverse this rejection. Claims 18 – 20 are stated as being rejected due to their dependency on claim 14. This rejection is unclear. Does this mean that they are allowable otherwise? Clarification is requested.

The Examiner cites a number of factors to indicate that the specification is deficient in its ability to essentially teach how to make and how to use the compounds of the present invention in the activities as claimed herein.

Claim 6 is not a method of determining inhibition as suggested by the Examiner. It is specifically a method or process of actually having the compound bind to an acetylcholine receptor in a mammal. As previously noted, this method is not tied to the treatment of a particular disease state or respiratory condition. The specification does provide more than ample support for such a claim. The second binding assay, page 6, lines 23 to 30 that provides for a pan-muscarinic antagonism screening assay against the M1 to M5 acetylcholine receptors would be indicative of this response. This assay is a means to determine agonism or antagonism of each of the muscarinic receptors. The skilled artisan would readily understand the significance of this assay and the potential limitations of compounds tested therein. This is a well known art recognized assay.

The first and the third described assay, appearing on page 5, lines 29 to 32, page 6, lines 1 to 21; and pages 7, lines 1 to 32, and page 8 lines 1 to 32, are also art recognized variations on accepted *in vitro* assays. The fourth assay contained in the specification is directed to *in vivo* inhibition. The "Methacholine-induced bronchoconstriction –potency and duration of action" assay on page 9, lines 1 to 24 will demonstrate inhibition of the muscarinic acetylcholine receptors *in vivo*. Again, this is an art recognized assay.

It appears that the Examiner is in concurrence with Applicants arguments that test data is not needed to prove sufficiency of the specification. The Examiner point being in that the specification is not sufficient to "use the invention". However, the Examiner has failed to show that the Application is not sufficient. The art is now suitably predictable in this field that use of *in vitro* antagonism data will establish utility of the invention.

As previously commented upon in Applicants prior response, the presently claimed compounds are already art recognized anti-cholinergic agents (see column 1, lines 20-26 of Zirkle, US 2,800,481). Therefore, the skilled artisan already has in their possession the knowledge that compounds of Formula (I) are useful as anti-cholinergics. Zirkle did not teach nor suggest the use of the compounds described therein for the treatment of disease states which require anticholinergic activity by the inhaled route of administration, suitably by the mouth, with a dry powder inhalation composition. The instant specification provides the skilled artisan four (4) assays directly related to supporting the method claims herein.

The specification provides for formulation details, amounts, how to use/administer such (dry powder formulations) of compounds of Formula (I), and reference additional patents on the various devices for such formulations.

"The enablement requirement is satisfied when one skilled in the art, after reading the specification, could practice the claimed invention without undue experimentation." *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003), citing *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988). Clearly, one of ordinary skill in the art would be able to synthesize a wide range of compounds of Formula (I) which are within the scope of the genus. This has been satisfied by the USPTO's allowance of the compounds of Formula (I) in US 2,800,478.

The specification also provides details on what the compounds are useful for, e.g. treatment of respiratory-tract disorders (page 1 to page 4, lines 1 to 4; page 5, lines 15 to 30 to page 9, lines 1 to 19. There are a large number of anticholinergic compounds in the art prior to the filing of this application which inhibit acetylcholine induced response and are deemed to be muscarinic antagonists. In fact, there are several on the market in the United States.

Applicant's invention is the novel use of these compounds as a composition for delivery to the lungs, whether it is via the oral inhalation route or nasal delivery. The

application provides a significant discussion on the various inhalers and formulation details therein. Consequently, it is believed that one of ordinary skill in the art is provided with sufficient information to also be able to use the compounds of Formula (I).

As noted, there may not even be a requirement to have any working embodiments in order to satisfy the requirements of § 112, first paragraph, even in the chemical arts, as evidenced by the decision in *In re Strahilevitz*, 668 F.2d 1229, 212 U.S.P.Q. 561 (CCPA 1982). In this case, Applicants had described the invention with specificity, but had not disclosed even a single operative embodiment. The court acknowledged that the claims at issue were extremely broad, yet the court reversed the Board's holding of nonenablement, having been persuaded by Strahilevitz that the invention consisted in combining known prior art techniques. Pointing out that § 112 does not require working examples (though they may be desirable in complex technologies), the court found the broad claims enabled throughout their scope. In *Strahilevitz*, Applicants were able to obtain broad claims to methods for removing haptens from blood, despite the fact that no working examples were disclosed, because the evidence of record established that the prior art had taught methods that, when combined together according to the teachings of the specification, could be used to make the claimed invention.

The MPEP 2164.01(c) on How to Use the Claimed Invention also clearly contemplates that a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of administration are known and contemplated, and that 25 USC §112 is thereby satisfied. The state of the art, taken with Applicants specification is sufficient within the context of M3 receptors antagonists to be enabled.

By law a patent application is presumptively enabled when filed. That is, during examination, "[a]s a matter of Patent Office practice . . . a specification . . . must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 439 F.2d at 223, 169 U.S.P.Q. at 369.

Moreover,

> . . . it is incumbent upon the Patent Office, whenever a rejection on [grounds of enablement] is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

Id. at 224, 169 U.S.P.Q. at 369-70.

Since the PTO bears the initial burden of challenging the presumed utility of an invention, it must produce sufficient evidence that one of ordinary skill in the art would have reason to doubt the claimed utility of the invention.

One of skill in the art, in combination with the submitted references as well as the state of the art would not question the claimed utility of the compounds described and claimed herein. The nature of the applicants' invention itself would also not tend to cause one skilled in the art to doubt its usefulness. Dosing is clearly within the skill of the artisan.

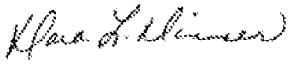
Applicants further dispute the level of skill in the art as necessarily being an individual with "a PhD, and possibly an MD, and several years of research experience". (See page 4, 1rst ¶, Office Action). There is no basis for a determination of this level of skill and seems to be a matter of random choice, unsupported by the Examiner. Further, in this listing of items, point g) on unpredictability for receptor inhibition has believed been specifically addressed by the previously known fact that these compounds have already been determined to be muscarinic antagonists.

The Examiner also comments on page 4, last line first paragraph that there is no formulation data to support the duration of action of claims 11 through 13 on 1mg dosages. Duration of action for an inhaled muscarinic compound is not due to formulation details as the Examiner appears to be alleging, but to the pharmacokinetics of the drug, e.g. what the body does to the drug. It is desirable to have a drug which can be dosed once or twice a day rather than three to four times a day.

In view of the remarks herein, reconsideration and withdrawal of the rejection to the claims under 35 USC §112, is respectfully requested.

It is believed that the claims, as amended, are now all in condition for allowance. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. It is not believed that this paper should cause any additional fees or charges to be required, other than expressly provided for already. However, if this is not the case, the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



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